REMARKS

Claims 11-30 are pending in the application. Claims 13-19 and 24-30 are withdrawn from consideration. Claims 11, 12 and 20-23 are rejected.

After entry of the amendment, claims 12, 22 and 23 will additionally be canceled.

The Examiner is thanked for agreeing to rejoin Group II claims when Group I claims are found allowable.

The first paragraph of the specification has been amended to update and correct the related application information.

Claim 11 has been amended to delete an alternative embodiment of the claimed polypeptide.

Claim Rejections - 35 U.S.C. §§ 101 and 112, First Paragraph

1. Claims 11, 12 and 20-23 are rejected under 35 U.S.C. § 101 because the claimed invention allegedly is not supported by either a specific and substantial asserted utility or a well established utility.

The Examiner asserts that even though the evidence is convincing that the claimed polypeptides are probably receptors in the TNFR family, this is insufficient to establish a specific and substantial utility. The Examiner asserts that the specific function of the OAF065 clone is not shown in the specification and that mere homology to other TNF receptors is not sufficient to find a correlation to a disease. In support, the Examiner cites Wallach, D., "TNF Ligand and TNF/NGF Receptor Families."

For the following reasons, the rejection is traversed, respectfully.

In the specification, there is a description of the functions of OAF065. The specification states that "it is considered that the polypeptide of the invention and a cDNA molecule which encodes the polypeptide will show one or more of the effects or biological activities (--abreviated--) concerning (I) differentiation, proliferation, growth, survival or (Ia) cell death of hematopoietic, immune and nerve system cells, (II) immune system functions, (III) proliferation and growth of tumor, (IV) inflammations, (V) bone metabolism etc." (lines 5-12, page 17).

The numbers (I), (II), (III), (IV) and (V) are added for reference.

Re: Disclosure of the activity in the specification

The clone OAF065 has multiple functions.

The functions that relate to (I), (II) and (IV) are demonstrated in the Rule 132 Declaration submitted herewith. The experimentation establishes that the clone OAF065 has the growth activity and differentiation activity of nerve system cells (which belongs to (I)), an activity of inhibiting production of cytokine in the immune system and an activity of inhibiting acceleration production of cytokine in inflammation (which belongs to each of (II) and (IV)).

Furthermore, the clone has cell death activity (which belongs to (Ia)) by analogy to the protein of Eby *et al* and the clone has tumor growth activity (which belongs to (III)) as is evident from Spanjaard *et al.* (copies of Eby et al. and Spanjaard et al. are submitted herewith).

Eby et al. teaches that a new TNF receptor that induces apoptosis can be obtained although it does not have a death domain. Usually, apoptosis is mediated by a caspase

pathway. However, TAJ does not mediate it. In mice, it is usually expressed in the embryonic stage. Thus, the receptor is expected to relate to apoptosis in organogenetic terms.

The receptor induces cell death without going through the caspase pathway. Since the TNFR family has a death domain, it has been thought that apoptosis occurs from the caspase pathway by going through the death domain as shown in the attached Figure. It has been thought that there is a viable route by activation of NFxB after going through from TRAF's to IKK pathway. The receptor is a factor that can induce apoptosis other than by this route.

In line 10 on page 17 of the specification of the present application, there is a description of "cell death". Apoptosis is one kind of cell death.

Spanjaard et al. teaches that "TROY" is an useful biomarker of melanoma. "TROY" is known as a factor that induces apoptosis. The publication discloses for the first time that it can be a biomarker. As described in Table 1, diagnosis with extremely high probability can be carried out by using it.

"TROY" is not expressed in normal melanocytes. However, it is specifically and definitely expressed in melanoma. Thus, it can be a marker. Additionally, in the left column on page 1308, it is indicated that "TROY" accelerates melanoma proliferation.

In the right column on page 1308, there is a general description that "TROY" actually induces paraptosis and that "TROY" is involved in embryonic development and is expressed in specific organs in adults although it does not have a death domain.

As described above, description in the specification that the polypeptide of the invention and cDNA molecule which encodes the polypeptide concern (III) proliferation and growth of tumor is demonstrated to be true.

Accordingly, multiple functions of the clone are disclosed in the specification, and the clone OAF065 has multiple activities of (I), (II), (III) and (IV), as described above.

Furthermore, OAF065 belongs to the TNF family. The clone OAF065 is known as TNFRSF-19. The Human Genome Organization (HUGO) discloses OAF065 in the chart of TNFRSF families (copies of the HUGO homepage and the HUGO chart are submitted herewith). TNFRSF-19 is thought to be a factor that is capable of inducing cell death. Additionally, since it is largely expressed in embryonic cells, it is expected to have a role in organizing cells by inducing cell death in un-needed parts. By using alignments (copies submitted herewith), Applicants have also shown that clone OAF065, TROY(NP_061117) and TNFRSF-19 (HUGO_AB040434) are essentially the same protein. Although there are some different amino acids, they are essentially the same.

Thus, the specification clearly discloses that the clone will be a member of the TNF family. The specification describes a sufficient number of functions of OAF065. The clone has the functions the inventors expected. And, the clone is recognized officially as a member of the TNF receptor family.

Accordingly, the Examiner is requested, respectfully to reconsider and remove this rejection.

2. Claims 11, 12 and 20-23 are also rejected under 35 U.S.C. § 112, first paragraph as lacking enablement. The Examiner asserts that absent either a specific and substantial asserted utility or a well established utility, one skilled in the art would not know how to use the claimed invention.

This rejection is traversed, respectfully, because the claims meet 35 U.S.C. § 101 as described above.

3. Claims 11, 22 and 23 are rejected under 35 U.S.C. § 112, first paragraph as lacking written description support in the specification.

Specifically the Examiner asserts that there is no written description for polypeptides having at least 95% homology with a protein of SEQ ID NOS: 4 or 8.

Claim 11 has been amended to delete the embodiment of the homologous polypeptide. Claims 22 and 23 have been canceled, thus making the rejection moot as to these claims.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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